Amendments to the Claims

Amendments to the claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims

1. (original) An isolated polynucleotide comprising the sequence of any one of SEQ ID Nos: 1-48, 52-64, 66, 68-84, 86, 88-93, 101-131.

2. (original) An isolated polynucleotide the expression of which is modulated in neural cells subjected to neurotoxic stress having the sequence of:
   (a) any one of SEQ ID NOs: 1-131
   (b) a naturally-occurring polynucleotide comprising a sequence of (a); or
   (c) a naturally-occurring polynucleotide having at least 70% identity with a naturally-occurring polynucleotide of (b) and, in naturally-occurring neural cells, has its expression modulated when the cells are subjected to neurotoxic stress;
   (d) a naturally-occurring polynucleotide capable of hybridizing under moderately stringent conditions to a naturally-occurring polynucleotide of (b) and, in naturally-occurring neural cells, has its expression modulated when the cells are subjected to neurotoxic stress;
   (e) a fragment of a polynucleotide of (a), (b), (c) or (d) having at least 20 nucleotides; or
   (f) a polynucleotide sequence complementary to a polynucleotide of (a), (b), (c), (d) or (e).

3. (original) The isolated polynucleotide of claim 2, the expression of which is modulated in neural cells subjected

to neurotoxic stress having the sequence of:

(a) any one of SEQ ID NOs: 1-48, 52-64, 66, 68-84, 86, 88-93, 101-131;

(b) a naturally-occurring polynucleotide comprising a sequence of (a); or

(c) a naturally-occurring polynucleotide having at least 70% identity with a naturally-occurring polynucleotide of (b) and, in naturally-occurring neural cells, has its expression modulated when the cells are subjected to neurotoxic stress;

(d) a naturally-occurring polynucleotide capable of hybridizing under moderately stringent conditions to a naturally-occurring polynucleotide of (b) and, in naturally-occurring neural cells, has its expression modulated when the cells are subjected to neurotoxic stress;

(e) a fragment of a polynucleotide of (a), (b), (c) or (d) having at least 20 nucleotides; or

(f) a polynucleotide sequence complementary to a polynucleotide of (a), (b), (c), (d) or (e).

4. (original) The isolated polynucleotide of claim 2 the expression of which is modulated in neural cells subjected to neurotoxic stress having the sequence of:

(a) any one of SEQ ID NOs: 49-51, 65, 67, 85, 87, 94-100;

(b) a naturally-occurring polynucleotide comprising a sequence of (a); or

(c) a naturally-occurring polynucleotide having at least 70% identity with a naturally-occurring polynucleotide of (b) and, in naturally-occurring neural cells, has its expression modulated when the cells are subjected to neurotoxic stress;

(d) a naturally-occurring polynucleotide capable of hybridizing under moderately stringent conditions to a naturally-occurring polynucleotide of (b) and, in

naturally-occurring neural cells, has its expression modulated when the cells are subjected to neurotoxic stress;

(e) a fragment of a polynucleotide of (a), (b), (c) or (d) having at least 20 nucleotides; or

(f) a polynucleotide sequence complementary to a polynucleotide of (a), (b), (c), (d) or (e).

5. (original) The isolated polynucleotide in accordance with claim 2 comprising a strand of a full-length cDNA.

6. (original) The isolated polynucleotide in accordance with claim 3 comprising a strand of a full-length cDNA.

7. (original) The isolated polynucleotide in accordance with claim 4 comprising a strand of a full-length cDNA.

8. (original) An isolated polypeptide the expression of which is modulated in neural cells subjected to neurotoxic stress, comprising a protein encoded by a full length cDNA in accordance with claim 5, a variant which has an amino acid sequence having at least 70% identity to said protein and retains the biological activity thereof, or a fragment of said protein or variant which retains the biological activity thereof, or a functional derivative or salt of said protein, variant or fragment.

9. (original) An isolated polypeptide the expression of which is modulated in neural cells subjected to neurotoxic stress, comprising a protein encoded by a full length cDNA in accordance with claim 6, a variant which has an amino acid sequence having at least 70% identity to said protein and retains the biological activity thereof, or a fragment of said protein or variant which retains the biological activity thereof, or a functional derivative or salt of said protein, variant or fragment.

10. (original) An isolated polypeptide the expression of which is modulated in neural cells subjected to neurotoxic stress, comprising a protein encoded by a full length cDNA in accordance with claim 7, a variant which has an amino acid sequence having at least 70% identity to said protein and retains the biological activity thereof, or a fragment of said protein or variant which retains the biological activity thereof, or a functional derivative or salt of said protein, variant or fragment.

11. (original) A molecule which comprises the antigen-binding portion of an antibody specific for a protein, variant or fragment in accordance with claim 8.

12. (original) A molecule which comprises the antigen-binding portion of an antibody specific for a protein, variant or fragment in accordance with claim 10.

13. (original) A method for diagnosing cells which have been subjected to a neurotoxic insult, hypoxia and/or ischemia, comprising assaying for RNA comprising a sequence of any one of SEQ ID NOs:1-131 or for the expression product of a gene in which one of said sequences is a part, the amount of said RNA or expression product as compared to a control indicating the likelihood that such cells have been subjected to hypoxia or ischemia.

14. (original) The method according to claim 13 for diagnosing cells which have been subjected to a neurotoxic insult, hypoxia and/or ischemia, wherein said RNA comprises a sequence of any one of SEQ ID NOs:49, 50, 51, 65, 67, 85, 87, 94-100

15. (original) The method according to claim 14 for diagnosing

cells which have been subjected to a neurotoxic insult, hypoxia and/or ischemia, wherein said RNA comprises a sequence of SEQ ID NOs: 65, or 94

16. (original) A method of screening for a neuroprotective compound comprising testing the ability of the compound to upregulate or downregulate a gene which is transcribed to an RNA containing a sequence of any of SEQ ID NOs: 1-131.

17. (original) The method of claim 16 of screening for a neuroprotective compound comprising testing the ability of the compound to upregulate or downregulate a gene which is transcribed to an RNA containing a sequence of any of SEQ ID NOs: 49, 50, 51, 65, 67, 85, 87 and 94-100.

18. (original) The method of claim 17 wherein the compound is capable of downregulating the transcription of SEQ ID No:94 or KIAA0538.

19. (original) The method of claim 17 wherein the compound is capable of upregulating the transcription of SEQ ID No:65 or KIAA0284 .

20. (currently amended) A method of identifying a neuroprotective compound comprising testing the ability of the compound to inhibit or enhance the activity of a polypeptide which is encoded by a nucleic acid which has a sequence of any of SEQ ID NOs: 1-131, compared to a control.

21. (currently amended) The method of claim 20 of identifying a neuroprotective compound comprising testing the ability of the compound to inhibit or enhance the activity of a polypeptide which is encoded by a nucleic acid which has a sequence of any of SEQ ID NOs: 49, 50, 51, 65, 67, 85, 87 and 94-100.

22. (original) The method of claim 21 wherein the compound is screened for the ability to inhibit a Ca^{2+} promoted Ras inactivator encoded by a member of the KIAA0538 gene family.

23. (original) A process for identifying a neuroprotective compound which specifically inhibits the polypeptide product of KIAA0538 gene which comprises:

(a) contacting cells expressing DNA encoding the KIAA0538 gene under conditions permitting expression of the DNA; and

(b) determining if the compound inhibits the polypeptide as compared to a control.

24. (original) The process of claim 23 wherein the cells are transfected with the KIAA0538 gene.

25. (original) The process of claim 23 wherein the cells endogenously express the KIAA0538 gene.

26. (original) The process of claim 23 wherein the cells are neuronal cells.

27. (original) A method of preparing a pharmaceutical composition which comprises the steps of:

(a) obtaining a compound which specifically inhibits the activity of the polypeptide product of the KIAA0538 gene; and

(b) admixing said compound with a pharmaceutically acceptable carrier.

28. (original) The method of claim 21 wherein the compound is

screened for the ability to activate or enhance the activity of a polypeptide encoded by KIAA0284.

29. (original) A method for screening for a compound which induces or inhibits apoptosis after exposure of neural cells to a neurotoxic insult, comprising the step of exposing the cells to the test compound and testing the change in expression of any one of the polynucleotides according to claim 2.

30. (original) The method according to claim 29 for screening for a compound which induces or inhibits apoptosis after exposure of neural cells to a neurotoxic insult, comprising the step of exposing the cells to the test compound and testing the change in expression of any one of the polynucleotides according to claim 4.

31. (original) The method according to claim 30, which comprises testing the compound for its ability to change the expression of any member of the KIAA0538 gene family.

32. (original) The method according to claim 30, which comprises testing the compound for its ability to change the expression of KIAA0284.

33. (currently amended) A method for identifying a compound which induces or inhibits apoptosis after exposure of neural cells to a neurotoxic insult, comprising ~~the step of~~ exposing the cells to the test compound and testing the change in expression of a polypeptide encoded by a nucleic acid which has a sequence as shown in any one of the ~~polypeptides~~ polynucleotides according to claim 7, as compared to a control.

34. (original) The method of claim 33 for identifying a compound

which induces or inhibits apoptosis after exposure of neural cells to a neurotoxic insult, comprising the step of exposing the cells to the test compound and testing the change in activity of any one of the polypeptides according to claim 8, as compared to a control.

35. (original) The method of claim 34 wherein the compound is screened for the ability to inhibit a Ca^{2+} promoted Ras inactivator encoded by a member of the KIAA0538 gene family.

36. (original) A method of identifying a compound capable of exerting a neuroprotective effect that ameliorates or diminishes the damage induced by a neurotoxic insult, comprising the step of screening for the ability of the compound to alter the level of expression of a polynucleotide according to claim 2, compared to a control.

37. (original) The method of claim 36 of screening for a compound capable of exerting a neuroprotective effect that ameliorates or diminishes the damage induced by a neurotoxic insult, comprising the step of screening for the ability of the compound to alter the level of expression of a polynucleotide according to claim 4.

38. (original) The method according to claim 37, which comprises testing the compound for its ability to inhibit the expression of any member of the KIAA0538 gene family.

39. (original) A method of identifying a compound capable of exerting a neuroprotective effect that ameliorates or diminishes the damage induced by a neurotoxic insult, comprising the step of screening for the ability of the compound to alter the activity of any one of the polypeptides according to claim 8, compared to a control.

40. (original) A method of identifying a compound capable of exerting a neuroprotective effect that ameliorates or diminishes the damage induced by a neurotoxic insult, comprising the step of screening for the ability of the compound to alter the activity of any one of the polypeptides according to claim 10.

41. (original) The method of claim 40 wherein the compound is screened for its ability to inhibit the activity of a Ca^{2+} promoted Ras inactivator encoded by a member of the KIAA0538 gene family

42. (original) Antisense DNA of a length sufficient to prevent transcription and/or translation of a gene, comprising a sequence which is complementary to a portion of a gene of which a sequence of SEQ ID NO:94 is a part.

43. (original) The antisense DNA of claim 42 of a length sufficient to prevent transcription and/or translation of a gene, comprising a sequence which is complementary to a portion of a gene of the KIAA0538 gene family.

44. (original) In a method for screening drugs which up-regulate or downregulate a gene, the improvement wherein said gene is a gene which is transcribed to an RNA containing a sequence in accordance with claim 2.

45. (original) In a method for screening drugs which up-regulate or downregulate a gene, the improvement wherein said gene is a gene which is transcribed to an RNA containing a sequence in accordance with claim 4.